Dempsey, Walla (NIH/NIAID) [E]

From: Garry, Robert F <rfgarry@tulane.edu>
Sent: Wednesday, January 7, 2015 11:25 AM
To: Taylor, Christopher (NIH/NIAID) [E]; Repik, Patricia (NIH/NIAID) [E]; Dempsey, Walla (NIH/NIAID) [E]
Subject: Re: Dr Khan rose bowl float - update

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Chris,

Thank you very much for the video!

I'm heading back to Sierra Leone on Saturday.

It will never be the same without Dr. Khan, Mbalu, Alex, Fullah and our other lost heroes.

The team there [and here] is working harder than ever to honor their memories.

No Ebola cases in Kenema for several months. Lassa definitely picking up. Four Lassa patients are in in the rehabilitated Old Ward – The new Ward construction is proceeding rapidly.

Of course the situation in the west is still dire in terms of Ebola. On this trip (some VHFC people already in force) we're completing a large field test of the Ebola RDTs. FDA has the last set of data they requested, so I am hopeful that FDA will soon grant the EUA for the RDT.

We're also going to try to figure out why the Ebola RDTs are so sensitive [which is good], basically we pick up every qPCR positive sample except for those at the very limit of detection of qPCR, circa 35 cycles or about 10-100 genomes. I believe that there is a lot of free VP40 in the blood of patients which is giving us the sensitivity boost – we'll take it regardless.

Just a note on the sequencing efforts with Pardis. About 900 samples were sent to Tulane last month and these have been extracted [a team from Broad came to NOLa] and sent to Boston. Sequences are rolling off and will be deposited in the NCBI database as they are curated. Sequences are very interesting to say the least, but we really need more samples/sequences from other countries to complete the picture.

Pat, Walla and Chris - hope your New Year is are off to a great start.

Bob G.

Non-responsive

Repik, Patricia (NIH/NIAID) [E]

From: Dempsey, Walla (NIH/NIAID) [E]
Sent: Tuesday, December 16, 2014 1:44 PM
To: 'Garry, Robert F'; Repik, Patricia (NIH/NIAID) [E]
Subject: RE: Update [bob garry - ebola DX]

Bob.

This is good news. Have you notified the US embassy about the MOH requirement for use of your RDT? It might be prudent for you to do so. We will also notify through our channels.

Thanks,

Walla

Walla Dempsey, Ph.D.

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Virology Branch
Division of Microbiology and
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Phone: 240 292-4197 (direct)

Email: wdempsey@niaid.nih.gov

From: Garry, Robert F [mailto:rfgarry@tulane.edu]
Sent: Tuesday, December 16, 2014 1:19 PM
To: Repik, Patricia (NIH/NIAID) [E]; Dempsey, Walla (NIH/NIAID) [E]
Subject: Update

Hi Pat and Walla,

Thought it would be a good opportunity to update. Please share with appropriate folks at NIH as needed.

1. We have completed all the analytical testing of the RDT in BSL 2, 3 and 4, and have submitted our EUA application to the FDA after they came back with request for more data, including data on cross-reactivity with other filoviruses. UTMB (Giesbert/Cross) did the requested experiments. There is cross-reactivity with Sudan and Bundibugyo viruses, but not Reston virus. We provided this additional data to FDA last week. We have a conference call with the FDA later today and will get a progress report and learn if they want any additional testing. I' on my way to a funeral in Indiana, but will have feedback I'm sure.

2. We are still compiling clinical data in Sierra Leone on the Ebola RDTs, mainly at the Kenema Government Hospital in Kenema. The clinical performance continues to look very good compared to qPCR.

Non-responsive

Hope all is well,

Bob G.

Non-responsive

Dempsey, Walla (NIH/NIAID) [E]

Non-responsive

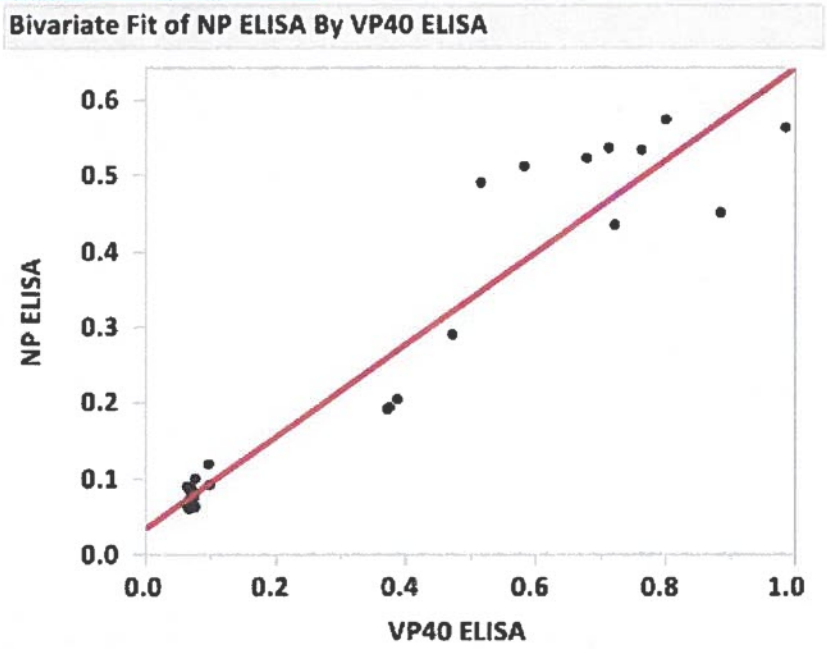
From: Garry, Robert F [mailto:rfgarry@tulane.edu]
Sent: Thursday, October 16, 2014 1:06 PM
To: Repik, Patricia (NIH/NIAID) [E]; Dempsey, Walla (NIH/NIAID) [E]
Cc: Laughlin, Catherine (NIH/NIAID) [E]
Subject: Re: Ebola RDT - follow-up

Having some internet issues in Salone, so here are the new RDT results as we have them.
Sorry these are just the positive samples. You can see that there were two samples on the sheet 008 that were invalid tests: 4209 (weak invalid control line) and 4217 that is badly hemolyzed. That leaves 28 samples run of which 26 positive on the RDT for sensitivity of 93% on this run.
Just got off the phone with Augustine and he ran 30 qPCR negative samples – all 30 of the suspects with negative qPCR were negative on the RDT. 100% specificity versus qPCR is holding.

Non-responsive

From: Garry, Robert F [mailto:rfgarry@tulane.edu]
Sent: Thursday, October 16, 2014 10:02 AM
To: Repik, Patricia (NIH/NIAID) [E]; Dempsey, Walla (NIH/NIAID) [E]
Subject: Ebola RDT - follow-up

EVRT-PP1-140930 (N=25, Serum)	5 Min Read	15 Min Read
Sensitivity (95th% CI)	84.6% (54.6 - 98.1)	92.3% (64.0 - 99.8)
Specificity (95th% CI)	100% (66.4 - 100)	100% (66.4 - 100)
Pos. Predictive Value (95th% CI)	100% (71.5 - 100)	100% (73.5 - 100)
Neg. Predictive Value (95th% CI)	81.8% (48.2 - 97.7)	90.0% (55.5 - 99.8)
Accuracy vs PCR (95th% CI)	90.9% (70.8 – 98.9)	95.5% (77.2 - 99.9)



Hi Pat and Walla,
Just a brief follow-up on the Ebola RDTs. The data got a bit better when CDC gave us their actual qPCR results. Two samples turned out not to actually be positive. We went from 80% sensitive that made us happy to 92% sensitive.
The sample that we did miss by RDT had the lowest virus load (less than ~10-100 genomes per ml) of any sample tested by qPCR. Again, that what we hope for. In a paper we have submitted to one of the medical journals we find that the CFR in people with fewer than 10^2 genomes/ml is significantly lower than in people with higher virus loads. These individuals are also likely to not be as "infectious."

Augustine also ran the samples on the recombinant EBOV ELISAs (NP capture or VP40 capture). The ReEBOV Antigen ELISA Tests exhibited a high degree of correlation ($R^2 = 0.922$ and signal bias of +36% by EBOV VP40), which tells us we're on the right track.

Also, Augustine is going to test our antibody capture (GP, Np and VP40 coated plates) ELISA. We already know these work well, but want to be positioned to say evaluate vaccines.

We know we need to increase numbers and more tests are in process on more samples – will keep you posted.

Bob

EBOV - VP-40 RDT

EBOV Positive Samples

[redacted] Test Worksheet

EURT-140920

Date: 10-Oct-14 Rapid Test Kit Lot: [redacted] Exp:

Sample	Sample Type (Circle One)	Dipstick Ctrl ↓ ↓ Test	Score 5min/15min/Ratio	Result (Circle One)	Initials
Pos Control			45	Pos/Neg/Retest	AG
Neg Control			00	Pos/Neg/Retest	AG
5525-1	S/P/WB/FS		23	Pos/Neg/Retest	AG
5532-1	S/P/WB/FS		24	Pos/Neg/Retest	AG
* 5579-1	S/P/WB/FS		00	Pos/Neg/Retest	AG
5571-1	S/P/WB/FS		12	Pos/Neg/Retest	AG
5529-1	S/P/WB/FS		12	Pos/Neg/Retest	AG
5530-1	S/P/WB/FS		01	Pos/Neg/Retest	AG
5527-1	S/P/WB/FS		34	Pos/Neg/Retest	AG
5510-1	S/P/WB/FS		12	Pos/Neg/Retest	AG
5516-1	S/P/WB/FS		01	Pos/Neg/Retest	AG
5565-1	S/P/WB/FS		34	Pos/Neg/Retest	AG
5584-1	S/P/WB/FS		34	Pos/Neg/Retest	AG
* 5522-1	S/P/WB/FS		00	Pos/Neg/Retest	AG
* 5223-1	S/P/WB/FS		00	Pos/Neg/Retest	AG
5585-1	S/P/WB/FS		23	Pos/Neg/Retest	AG
5590-1	S/P/WB/FS		23	Pos/Neg/Retest	AG
5570-1	S/P/WB/FS		13	Pos/Neg/Retest	AG

Read Visual

(Place dipstick here for photograph)

ReEBOV - VP-40 RDT EBOV Negative Samples

[redacted] Test Worksheet EVRT 140930

Date: 10 Oct-14 Rapid Test Kit Lot: [redacted] Exp:

Sample	Sample Type (Circle One)	Dipstick Ctrl ↓ ↓Test	Score 5min/15min/Ratio	Result (Circle One)	Initials
Pos Control			+ +	Pos/Neg/Retest	AGT
Neg Control			0 0	Pos/Neg/Retest	AGT
5578-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5513-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5515-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5521-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5555-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5588-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5517-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
[redacted]-064	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
5561-1	S/P/WB/FS		0 0	Pos/Neg/Retest	AGT
	S/P/WB/FS	[Place dipstick here for photograph]		Pos/Neg/Retest	
	S/P/WB/FS	[Place dipstick here for photograph]		Pos/Neg/Retest	
	S/P/WB/FS	[Place dipstick here for photograph]		Pos/Neg/Retest	
				Pos/Neg/Retest	

EVRT-PP1-140930 (N=25, Serum)	5 Min Read	15 Min Read
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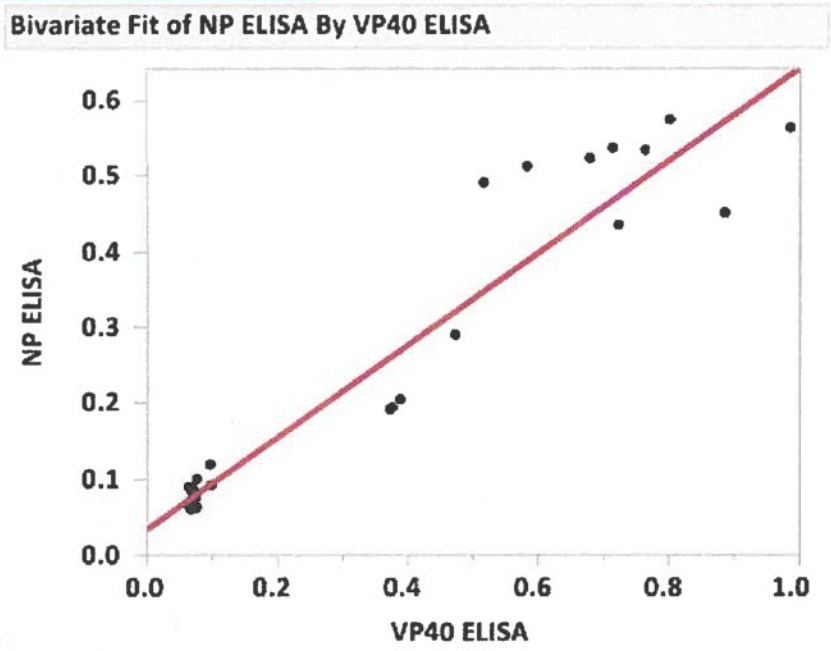

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Also, Augustine is going to test our antibody capture (GP, Np and VP40 coated plates) ELISA. We already know these work well, but want to be positioned to say evaluate vaccines.

We know we need to increase numbers and more tests are in process on more samples – will keep you posted.
Bob

Page 13 of 45 to Page 38 of 45

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Unpublished

of the Freedom of Information and Privacy Act

Repik, Patricia (NIH/NIAID) [E]

Non-responsive

From: <Garry>, Robert Garry <rfgarry@tulane.edu>
Date: Monday, October 13, 2014 8:32 AM
To: "Repik, Patricia (NIH/NIAID) [E]" <PRepik@niaid.nih.gov>, "Dempsey, Walla (NIH/NIAID) [E]" <WDEMPSEY@niaid.nih.gov>
Subject: Ebola RDTs

Hi Pat and Walla,

I just wanted to update you on the initial progress with the field testing of the Ebola RDT.

The results – though limited - were very good.

We got over 80% sensitivity and so far 100% specificity (no false positives).

The 80% is probably an underestimate as far as sensitivity as these were with banked samples. You can see the degradation of the samples. The hemolysis happens during transport. A fingerstick with fresh blood will be better. And, we do not know about precise virus load in the samples tested yet. Likely a false positive qPCR or two. More samples to be run and additional data about virus loads and outcomes is on the way.

WHO says the test must be positive anytime in the first 10 days of symptoms and allows for retesting, so I think we are there. If we miss a few cases on the first bleed with low virus loads (PCR does this too) retesting of symptomatics at 48 hours per WHO guidance is recommended.

Regardless, this level of sensitivity [80%] is what we were very much hoping for. This will allow effective testing at the village, neighborhood and household level. You don't need a test with 100% sensitivity to identify the "hotspots." Cases can be identified at the point of care and you need not wait 24-72 hours for results of qPCRat a central lab.

We probably dialed back the sensitivity a bit too much to avoid the false positives.

"Gen 2" and "gen 3" strips (working even better in the lab) are on the way to Kenema.

Let me know if you have any questions. Will keep you posted...

Bob

Robert F. Garry, PhD
Professor, Department of Microbiology and Immunology
Assistant Dean, Graduate Program in Biomedical Sciences
Tulane University School of Medicine, SL-38
1430 Tulane Avenue, JBJ568
New Orleans, LA 70118

EBOV - VP-40 RDT

EBOV Positive Samples

[redacted] Test Worksheet

EVRT-140930

Date: 10-Oct-14 Rapid Test Kit Lot: [redacted] Exp:

Sample	Sample Type (Circle One)	Dipstick Ctrl ↓ ↓ Test	Score 5min/15min/Ratio	Result (Circle One)	Initials
Pos Control			4 5	Pos/Neg/Retest	AG
Neg Control			0 0	Pos/Neg/Retest	AG
5525	S/P/WB/FS		2 3	Pos/Neg/Retest	AG
5532	S/P/WB/FS		2 4	Pos/Neg/Retest	AG
5579	S/P/WB/FS		0 0	Pos/Neg/Retest	AG
5571	S/P/WB/FS		1 2	Pos/Neg/Retest	AG
5529	S/P/WB/FS		1 2	Pos/Neg/Retest	AG
5530	S/P/WB/FS		0 1	Pos/Neg/Retest	AG
5527	S/P/WB/FS		3 4	Pos/Neg/Retest	AG
5510	S/P/WB/FS		1 2	Pos/Neg/Retest	AG
5516	S/P/WB/FS		0 1	Pos/Neg/Retest	AG
5565	S/P/WB/FS		3 4	Pos/Neg/Retest	AG
5584	S/P/WB/FS		3 4	Pos/Neg/Retest	AG
5522	S/P/WB/FS		0 0	Pos/Neg/Retest	AG
5223	S/P/WB/FS		0 0	Pos/Neg/Retest	AG
5585	S/P/WB/FS		2 1	Pos/Neg/Retest	AG
5590	S/P/WB/FS		2 3	Pos/Neg/Retest	AG
5570	S/P/WB/FS		1 3	Pos/Neg/Retest	AG

(Place dipstick here for photograph)

Visual

ReEBOV - VP-40 RDT EBOV Negative Samples

[illegible] Test Worksheet

Date: 10 Oct-14 Rapid Test Kit Lot: [illegible] EVRT 140930 Exp: _____

Sample	Sample Type (Circle One)	Dipstick Ctrl ↓ ↓ Test	Score 5min/15min/Ratio	Result (Circle One)	Initials
				Pos/Neg/Retest	
Pos Control			+ S	Pos/Neg/Retest	AG
Neg Control			D D	Pos/Neg/Retest	AG
5578	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5513	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5515	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5521	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5555	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5588	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5517	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
MSF-064	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
5561	(S) P/WB/FS		D D	Pos/Neg/Retest	AG
	S/P/WB/FS	[illegible]		Pos/Neg/Retest	
	S/P/WB/FS	[illegible]		Pos/Neg/Retest	
	S/P/WB/FS	[illegible]		Pos/Neg/Retest	
				Pos/Neg/Retest	

Repik, Patricia (NIH/NIAID) [E]

Non-responsive

From: Garry, Robert F [mailto:rfgarry@tulane.edu]
Sent: Wednesday, September 10, 2014 9:38 AM
To: Repik, Patricia (NIH/NIAID) [E]; Dempsey, Walla (NIH/NIAID) [E]; Laughlin, Catherine (NIH/NIAID) [E]; Ward, Lucy (NIH/NIAID) [E]
Subject: EBOV RDT

Dear Colleagues,

I wanted to briefly bring you up to date on our [VHFC] progress with EBOV rapid diagnostic tests.

We now have EBOV RDTs with a very good limit of detection, and very clean background (attached).

There's opportunity to optimize further and get at least another log of sensitivity, but this test is already very good (250 picogram sensitivity).

Obviously, we need to run the tests on actual patient samples, which needs to be done ASAP.

Ideally the rapid test would detect people with mild symptoms who are already infectious or about to become infectious.

If nothing else it could be deployed at airports.

I think an RDT could be deployed at the frontlines too.

The big problem with PCR (beyond false positives like Mambu proved to be) is you have to draw a sample, send it to the lab and wait at least 4-6 hours or longer for the result.

The RDT could be used on a group of villagers on the spot with the ability to identify at least 80% of the positives and their contacts.

Please let me know if you have questions. We're all meeting here in New Orleans in a few days to carefully sort out next steps.

Bob G.

Robert F. Garry, PhD
Professor, Department of Microbiology and Immunology
Assistant Dean, Graduate Program in Biomedical Sciences
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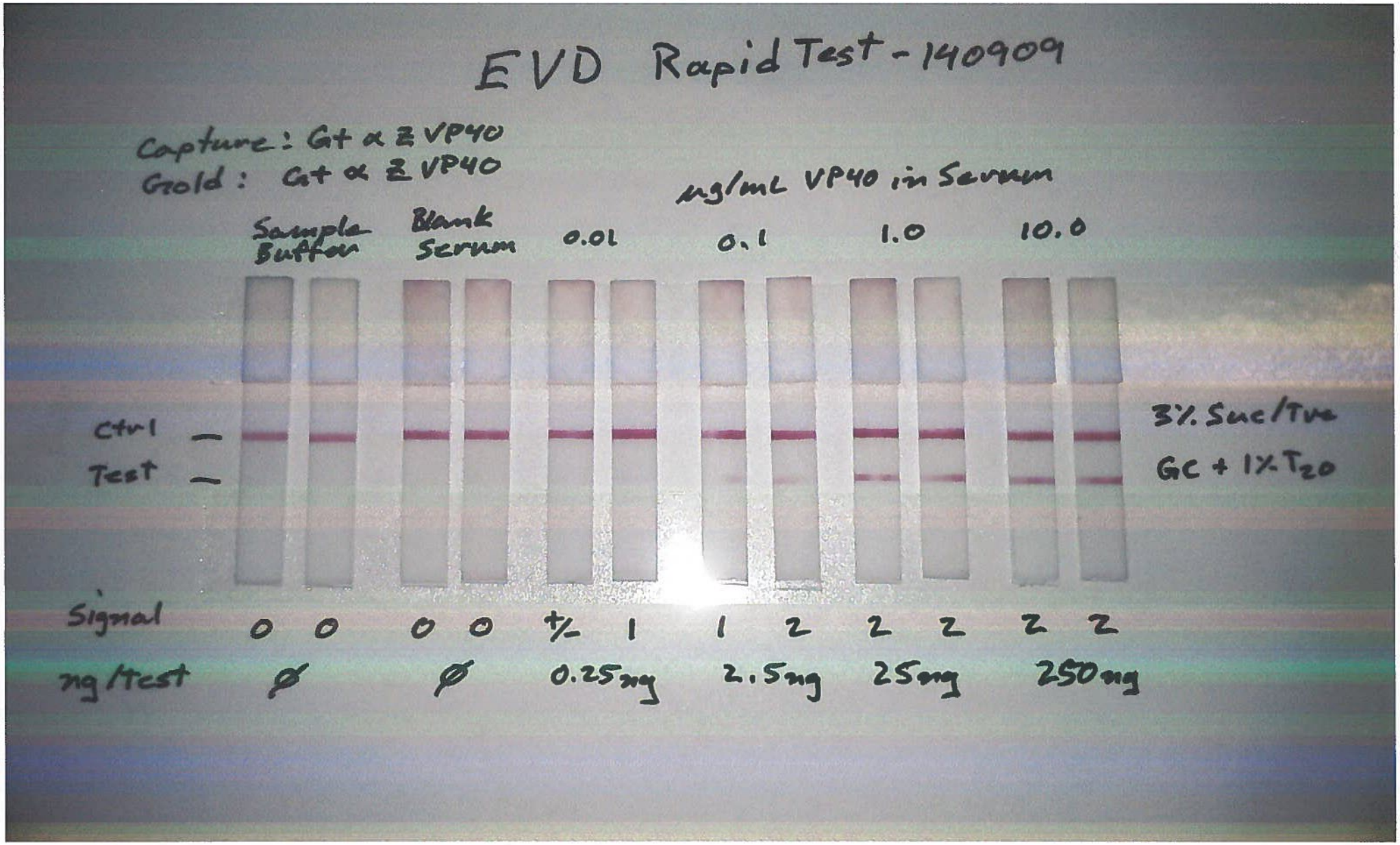
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Gold: Gt α Z VP40
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Sample Buffer
Blank Serum
0.01
0.1
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10.0
Ctrl
Test
3% Suc/Tre
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